OIPE JC98 MAY 21 2004 PATENT & TRADEMARK OFFICE

Appendix A

Claim Amendments

1-8. (Canceled)

9. (Canceled)

10. (Currently Amended) A method of predicting a therapeutically optimal drug dosage ~~and/or~~ or drug efficacy for a particular individual patient suffering from cancer in respect of genomic data, ~~including alleles and/or characteristic SNP patterns, of the particular patient,~~ the method comprising:

training a neural network on numerous examples of (i) genomic data ~~including~~ comprising alleles ~~and/or~~ or characteristic SNP patterns, and (ii) historical drug dosage results~~, including~~ comprising optimal drug dosages, for a multiplicity of patients suffering from cancer which historical drug dosage results are related to at least some of the genomic data so as to make a trained neural network that is fit~~, and that possesses a measure of goodness,~~ to map (i) genomic data for said cancer~~, including~~ comprising alleles ~~and/or~~ or characteristic SNP patterns, to (ii) drug dosage results

including optimal drug dosages effective to treat said cancer; and

exercising the trained neural network on the genomic data~~,~~ ~~including~~ comprising the alleles ~~and/or~~ or characteristic SNP patterns, of a particular individual patient suffering from cancer to predict an optimal drug dosage for the particular individual patient suffering from said cancer from among the optimal drug dosages to which the neural network was trained;

wherein said alleles or characteristic SNP patterns are selected from the group consisting of entire gene families, specific alleles, specific base pair sequences, locations and types of introns, nucleotide polymorphism, ethnicity, race, diet type, home region, occupation, viral levels, peptide levels, blood plasma levels, pharmacokinetic and pharmacodynamic parameters, and combinations thereof;

and wherein said historical drug dosage results are selected from the group consisting of presence of any of biological conditions, diseases, and characteristics, quantitative clinical measures of a patient, any presence of characteristics for which a genetic or environmental origin is either not clear or not uniquely defined, cost or performance functions calculated from values of multiple "real" clinical variables, and combinations thereof.

11-13. (Canceled)

14. (Previously Presented) The method according to ~~claims 9 or~~ claim 10

wherein the training is automated by computerized programmed operations using a genetic algorithm.

15. (Previously Presented) The method according to ~~claims 9 or~~ claim 10

wherein the training is automated by computerized programmed operations using a genetic algorithm reduced in computational complexity by including the steps of:

grouping alleles ~~and/or~~ or characteristic SNP patterns into families as are defined by (i) having similar expression patterns, or (ii) being turned on and off by another gene, or (ii) both having similar expression patterns and being turned on and off by the same gene; and

starting training of the neural network with the genetic algorithm by using the families so created as single inputs to the neural network, the training with the genetic algorithm continuing repetitively until, families of greater and lesser significance being identified, it becomes computationally

possible to train the neural network to genomic data consisting of individual alleles ~~and/or~~ or characteristic SNP patterns;

wherein partitioning of all alleles ~~and/or~~ or characteristic SNP patterns into families permits training of the neural network in a hierarchy of stages, first to the families and only then to the individual alleles ~~and/or~~ or characteristic SNP patterns.

16-26. (Canceled)

27. (New) The method of claim 10, wherein said cancer is breast cancer.

28. (New) The method of claim 10, wherein said characteristics for which a genetic or environmental origin is either not clear or not uniquely defined are selected from the group consisting of aggressive tendencies, sexual orientation, eating disorders, and combinations thereof.

29. (New) The method of claim 10, wherein said allele is TPMT.

30. (New) The method of claim 29, wherein said drug is a thiopurine drug.

31. (New) The method of claim 30, wherein said thiopurine drug is selected from the group consisting of mercaptopurine, azothioprene, thioguanine, and mixtures thereof.